The antibody-drug conjugate (ADC) loncastuximab tesirine (ADCT-402) targeting CD19 shows strong *in vitro* anti-lymphoma activity both as single agents and in combination

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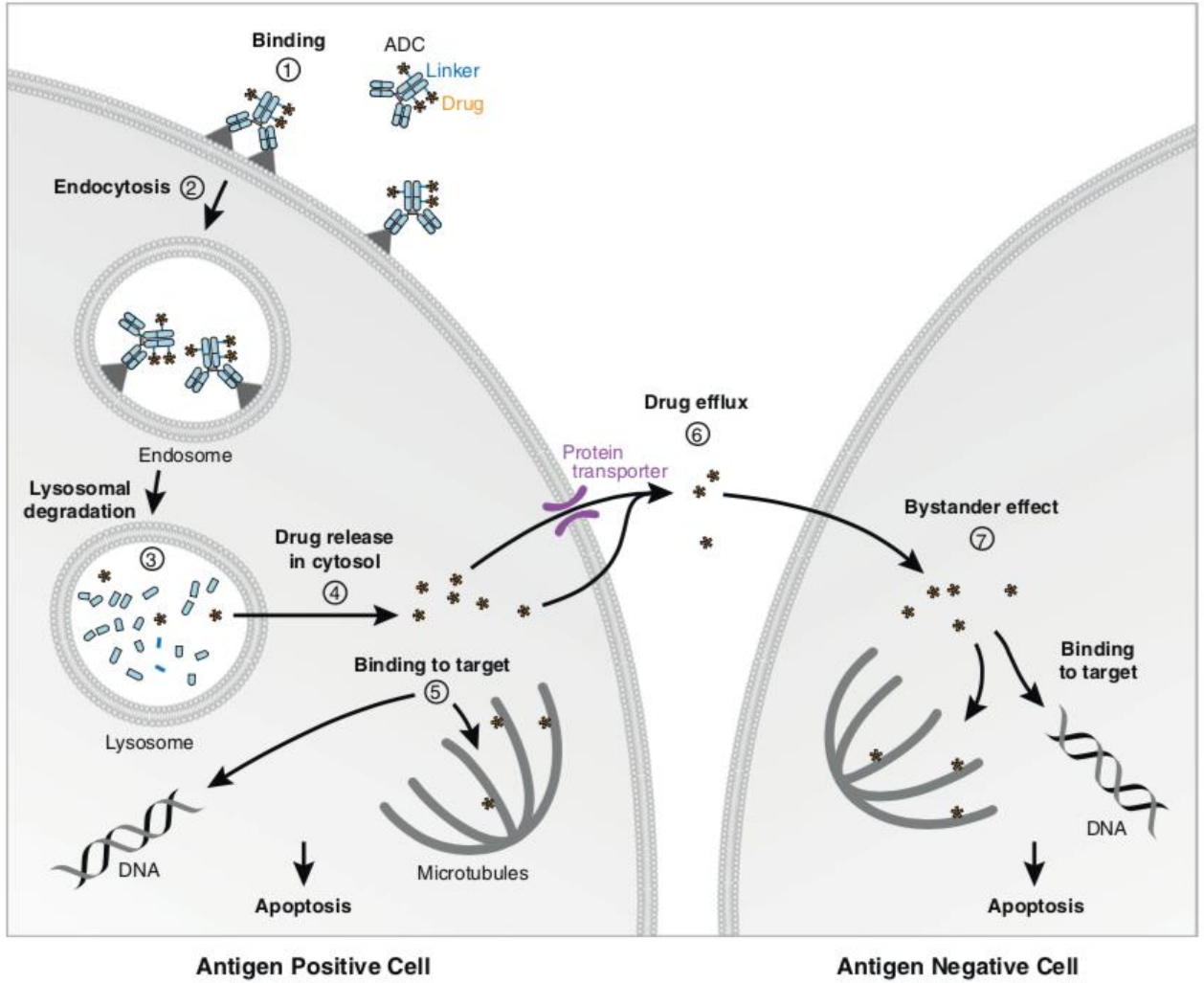
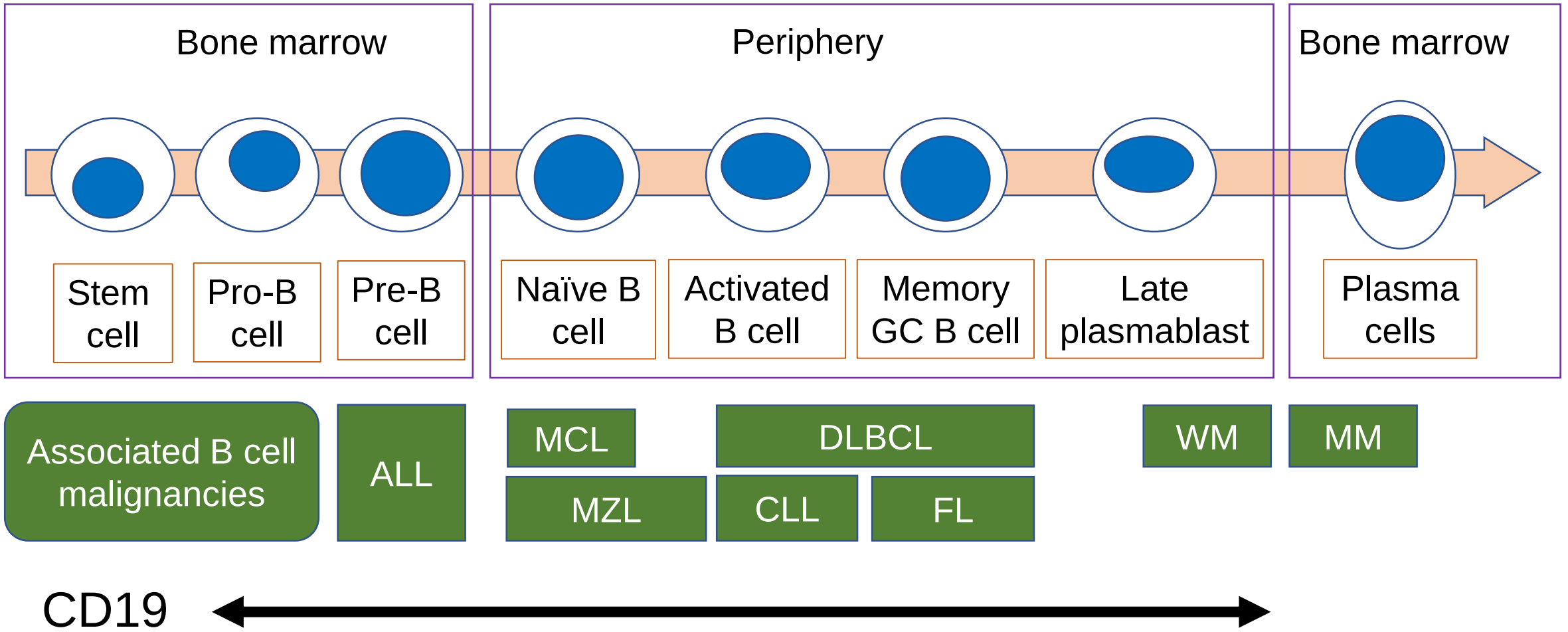
Antibody Drug Conjugate (ADC)



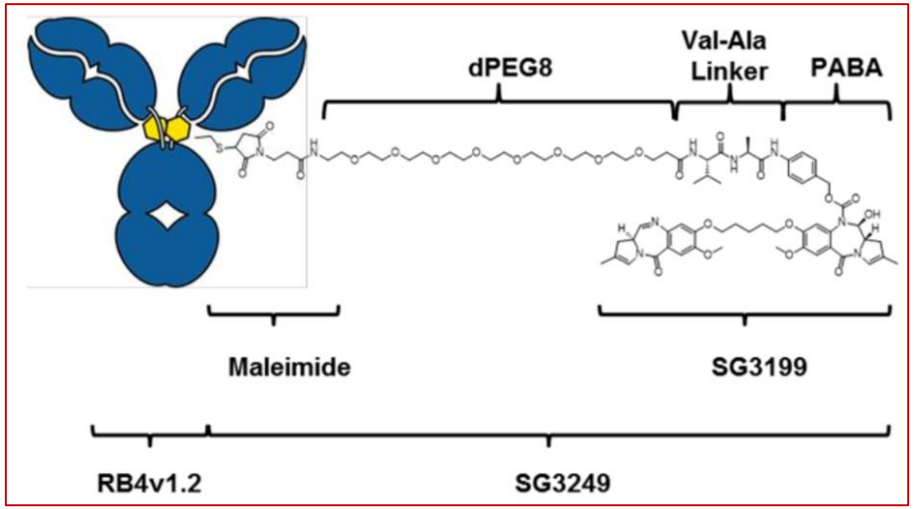
Chalouni and Doll, J Exp & Clin Cancer Res, 2018

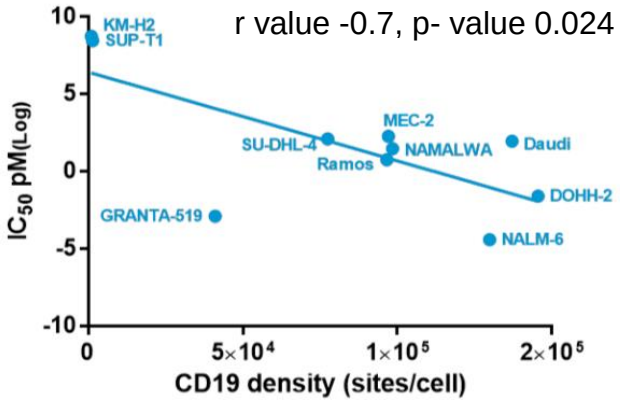
CD19: expressed across all B cell development stages

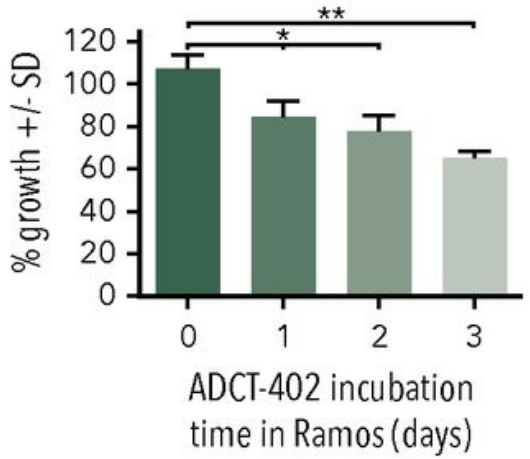


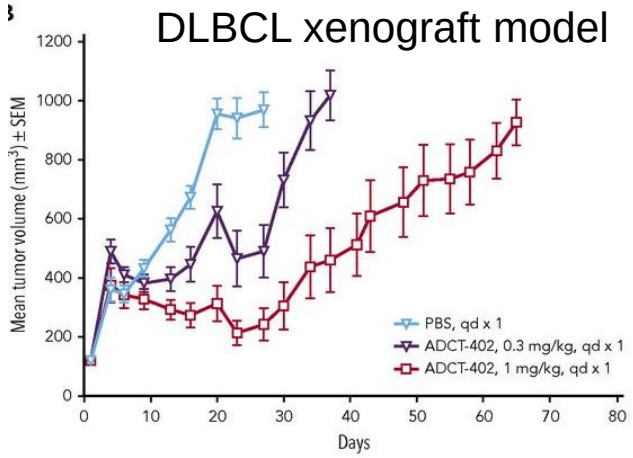
Adapted from Blanc V et al, CCR, 2011

Loncastuximab tesirine (ADCT-402) is a new anti-CD19 ADC active against hematological malignancies









Zammarchi F et al, Blood 2018

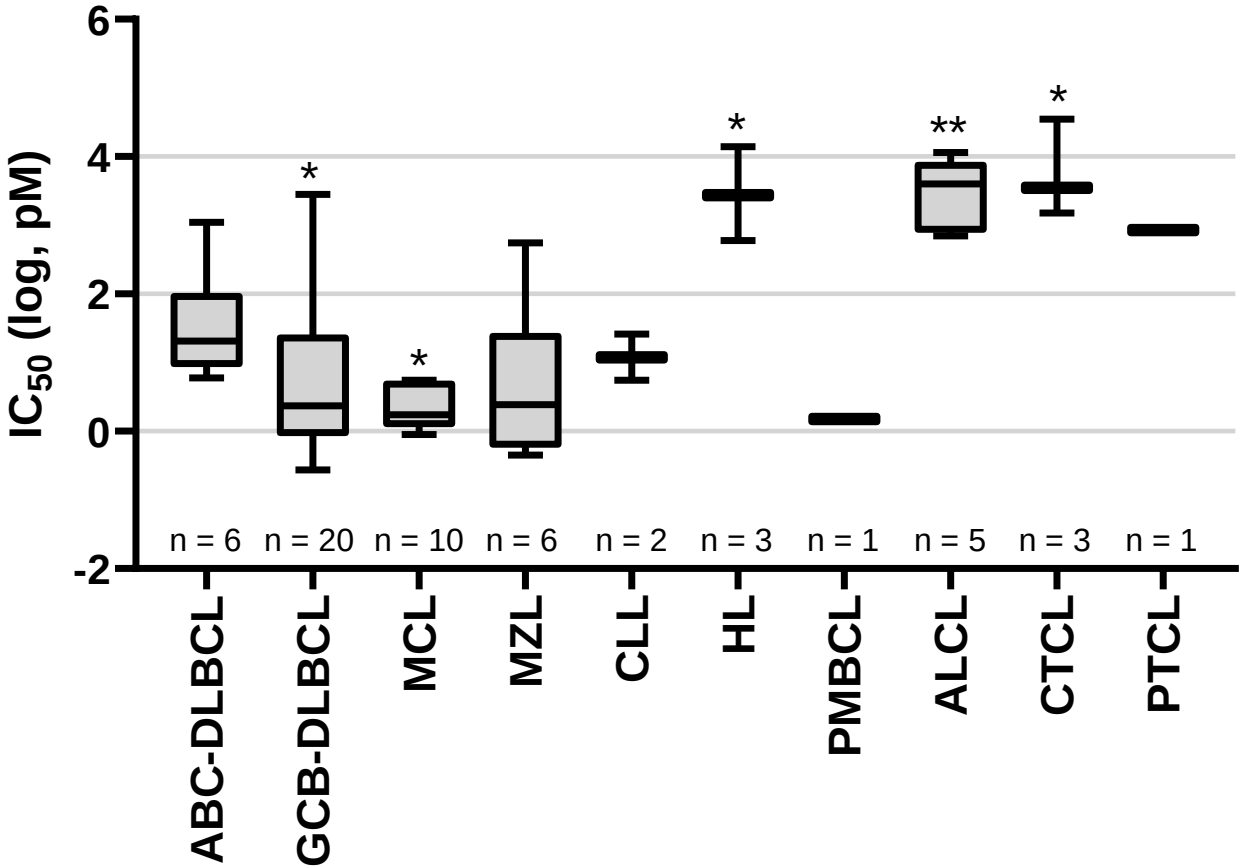
Clinical trials

NCT number	Study title	Phase	Status
NCT02669017	Dose-escalation Study to Evaluate the Tolerability, Safety, Pharmacokinetics, and Antitumor Activity of ADCT-402 in Patients With Relapsed or Refractory B-NHL	Phase 1	Completed *
NCT03589469	Study to Evaluate the Efficacy and Safety of Loncastuximab Tesirine in Patients With Relapsed or Refractory DLBCL	Phase 2	Recruiting
NCT03684694	Safety and Antitumor Activity Study of Loncastuximab Tesirine + Ibrutinib in DLBCL or MCL	Phase 1	Recruiting
NCT03685344	Safety and Antitumor Activity Study of Loncastuximab Tesirine and Durvalumab in DLBCL, MCL, or FL	Phase 1	Recruiting

* Oral (abstract 054) by J. Radford approximately one hour ago also here at the ICML

Data from www.clinicaltrial.gov

Activity on lymphoma cell lines

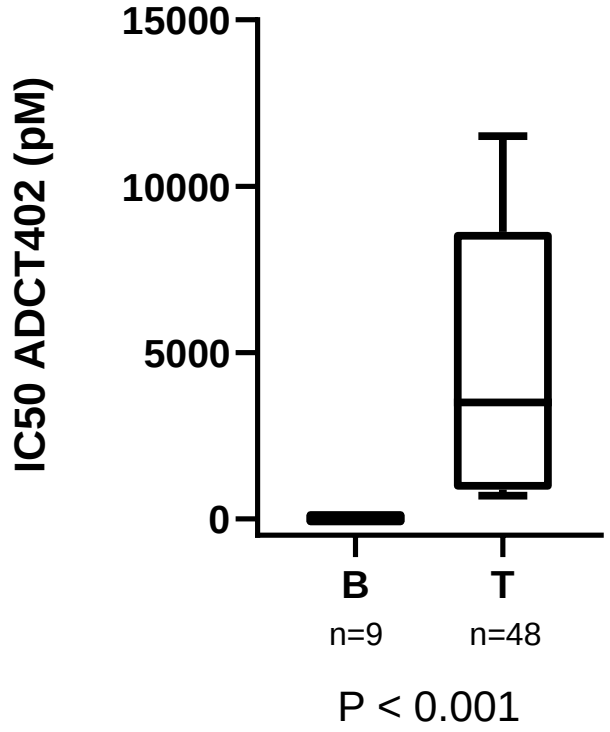


	Number of cell lines	Median IC50 (log, pM)	95% CI
ABC-DLBCL	6	1.3	0.8-3
GCB-DLBCL	20	0.4	0.1-1.1
MCL	10	0.2	0.0-0.7
MZL	6	0.4	-0.3-2.7
CLL	2	1.8	0.7-1.4
HL	3	3.4	2.8-4.1
PMBCL	1	0.1	n/a
ALCL	5	3.6	2.8-4
CTCL	3	3.5	3.2-4.5
PTCL	1	2.9	n/a

MTT proliferation assay and IC50 calculation on cell lines exposed (96h) to increasing ADCT-402 concentrations

*, P<0.05; **, P<0.01

Sensitivity to ADCT-402 is higher in B than T-cell lymphomas



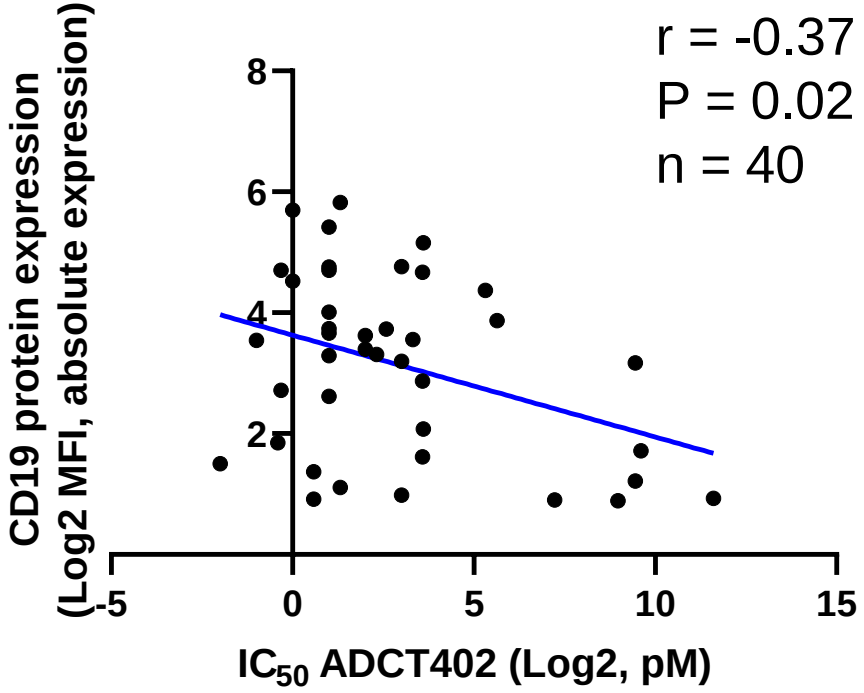
B-cell lymphoma (n=48)
median IC50=4 pM (95%C.I, 2-10 pM)

T-cell lymphoma (n=9)
median IC50=3.5 nM (95%C.I, 0.8-11 nM)

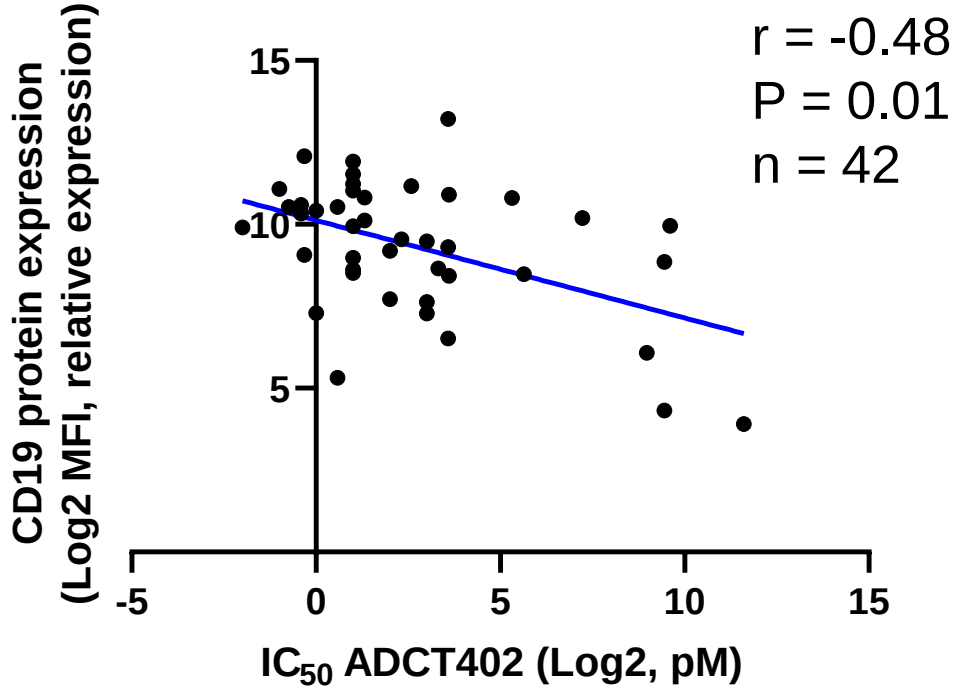
MTT proliferation assay and IC50 calculation on cell lines exposed (96h) to increasing ADCT-402 concentrations

ADCT-402 *in vitro* activity correlates with CD19 surface protein expression in B cell lines

MFI
absolute expression

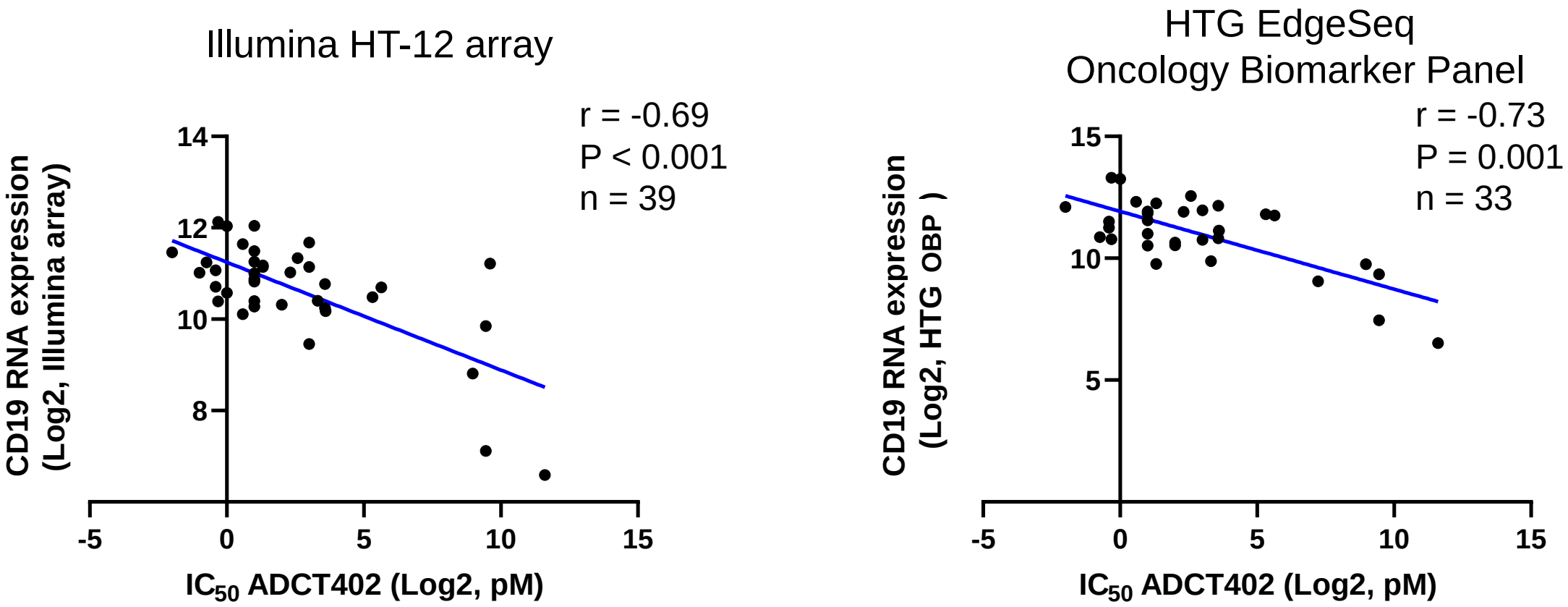


MFI
relative expression



Pearson correlation (r)

ADCT-402 *in vitro* activity correlates with CD19 RNA levels in B cell lines



Pearson correlation (r)

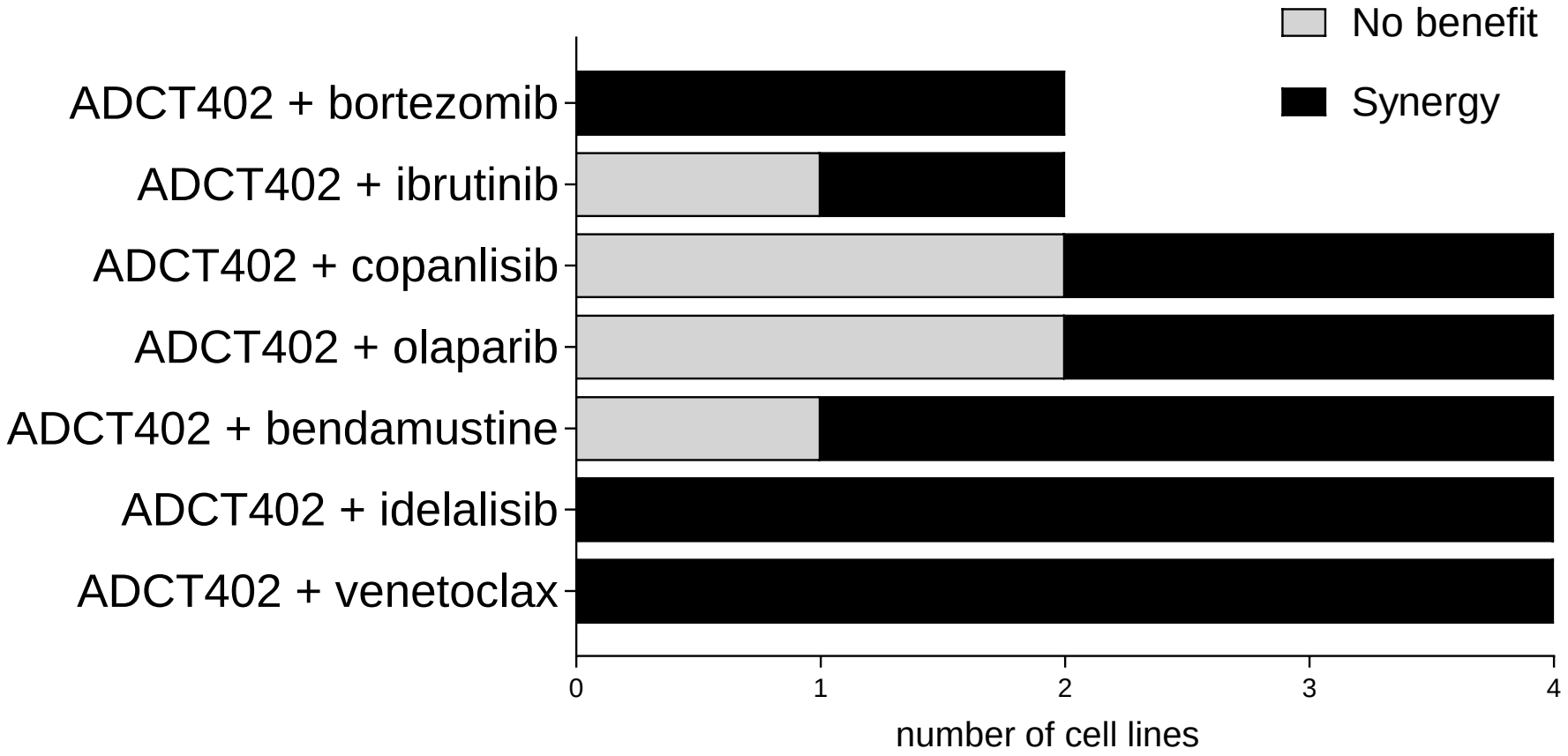
Drugs tested in combination with ADCT-402

Second drug	Target / MOA
venetoclax	BCL2 inhibitor
Ibrutinib *	BTK inhibitor
bendamustine	Chemotherapy agent
lenalidomide	Immunomodulator
copanlisib	PI3K inhibitor
idelalisib	PI3K δ inhibitor
olaparib	PARP inhibitor
bortezomib *	Proteasome inhibitor

* ABC only

MTT proliferation assay, 96h, 2 ABC – 2 GCB DLBCL cell lines
Synergy assessed by Chou-Talalay combination index (CI)
synergism CI<0.9, additive CI=0.9-1.1, antagonism/no benefit CI> 1.1

ADCT-402: best synergism with venetoclax, idelalisib and bendamustine



MTT proliferation assay, 96h, 2 ABC – 2 GCB DLBCL cell lines
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synergism CI<0.9, additive CI=0.9-1.1, antagonism/no benefit CI> 1.1

Conclusions

- ADCT-402 is strongly active *in vitro* in a wide panel of lymphoma cell lines
- ADCT-402 *in vitro* activity correlates with CD19 expression at protein and RNA level
- The results support the currently on-going clinical studies in relapsed/refractory DLBCL
- The novel combination data provide rational for further clinical development, such as combination with venetoclax, idelalisib and bendamustine.

Acknowledgments

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